Remarks

Applicants have now cancelled claim 1 and amended claims 11, 12, 15 and 16 in order to define the claimed method as preventing clotting induced by contact with surfaces in an extracorporeal blood circuit for a patient undergoing chronic, intermittent, extracorporeal blood treatment. This amendment limits the method to use with patients undergoing chronic, intermittent, extracorporeal blood treatment and cures an omission kindly identified by the Examiner in the Advisory Action, paper No. 10.

In the Example beginning line 3 on page 5 of the specification, the reported clinical study is performed in patients undergoing "chronic, intermittent haemodialysis." Haemodialysis is one of the uses of extracorporeal blood circuits, as listed in the first paragraph on page 3. It is also the purpose for which the method is claimed in original claim 4. Use of the method to prevent clotting as the result of contact with surfaces of extracorporeal blood circuits is reported in paragraph 2 on page 1 of the specification.

The significance of limiting the claimed method to treating patients undergoing chronic, intermittent, extracorporeal blood treatment is that these patients are

subject to repeated treatment occurring at intervals dictated by the extent of their disease, such as kidney disease being treated by dialysis. The claimed dosages are the dosages required for each treatment, they are not the daily dosages recited in the Petitou reference, which are administered every day to patients afflicted with thrombotic disorders.

The Examiner has referred to the first paragraph in column 5 of Petitou et al '829, where it is recited, "[f]or the treatment of venous thrombosis or for the inhibition of smooth muscle cell proliferation the compounds of the invention may be administered enterally or parenterally, and for humans preferably in a daily dosage of 0.001-10mg per kg body weight."

Petitou et al teach methods for treating thrombotic diseases by administering particular compounds every day. The present invention relates to preventing clotting caused by surface contact in an extracorporeal blood circuit of a patient undergoing chronic, intermittent, extracorporeal blood treatment. These are clinically, significantly different uses, as set forth in paragraph 2 on page 1 of the present specification:

"Blood clotting in extracorporeal blood circuits

needs to be prevented. Otherwise, blood coagulation occurs as soon as blood contacts artificial surfaces. As a remedy, usually unfractionated heperain (UFH) or low molecular weight heparins (LMWH) are used as anti-coagulants. Both UFH and LMWH have an effect on several stages of the blood coagulation cascade, both inhibiting factor Xa and thrombin (factor IIa)."

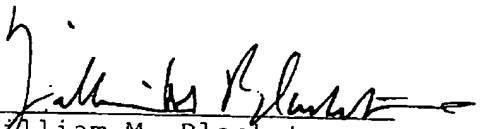
In paragraph 3 on the same page it is reported that the synthetic oligosaccharides, such as those used in the present invention, highly selectively inhibit factor Xa via anti-thrombin III (ATIII), but have no activity on thrombin. Thus, they do not function like the heparins conventionally used. Even so, applicants discovered that they inhibit thrombin formation in extracorporeal blood circuits.

It is submitted that the teaching of Petitou et al is clearly related to the treatment of venous thrombosis and the inhibition of smooth muscle cell proliferation. Nothing is suggested regarding coagulation induced by contact with synthetic surfaces. The ordinary practitioner would not find this disclosure to provide a reasonable assurance of success in preventing blood clotting in extracorporeal blood circuits of patients undergoing chronic, intermittent extracorporeal blood treatment.

In view of the above, with the present amendments to the claims, it is believed that claims 11-18 are in condition for allowance. Favorable action is solicited.

Should the Examiner consider that a conference would be helpful in advancing the prosecution of this application, she is invited to telephone Applicants' attorney at the number below.

Respectfully submitted,



William M. Blackstone
Attorney for Applicants
Registration No.: 29,772

Akzo Nobel Patent Department
Intervet Inc.
P.O. Box 318
Millsboro, DE 19966
Tel: (410) 464-0581
Sec: (302) 933-4027
Fax: (302) 934-4305

WMB:kmm